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EXAMINER	
SMITH HICKS,E	
ART UNIT	**PAPER NUMBER**
1741	7

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Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 09/416,680	Applicant(s) SCHEURING ET AL.	
	Examiner Erica Smith-Hicks	Art Unit 1741	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).

Status

1)☒ Responsive to communication(s) filed on *13 October 1999* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-9 and 11-51* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-9 and 11-51* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a)☐ All b)☐ Some * c)☐ None of the CERTIFIED copies of the priority documents have been:

1.☐ received.

2.☐ received in Application No. (Series Code / Serial Number) _____ .

3.☐ received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. & 119(e).

Attachment(s)

15)☒ Notice of References Cited (PTO-892)
16)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17)☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
18)☐ Interview Summary (PTO-413) Paper No(s). _____ .
19)☐ Notice of Informal Patent Application (PTO-152)
20)☐ Other:

DETAILED ACTION

This Office Action is in response to Applicant's Amendment dated July 27, 2000. The text of those sections of Title 35 USC not included in this Action can be found in the previous Office Action dated January 27, 2000. Claims 1-9 and 11-51 are pending in the instant application.

Claim Rejections - 35 USC § 102

1. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

2. Claims 1, 6-9, 11-15 and 47 are rejected under 35 U.S.C. 102(b) as being anticipated by SOUTHERN, US 5,667,667.

Claims 1 and 47 are rejected because SOUTHERN teaches a method for electrochemical placement of a material at a specific location on a porous substrate (glass col. 4, line 39) comprising providing a plurality of reaction locations on the porous substrate, each reaction location being individually electronically addressable and proximate to at least one molecule bearing at least one protected chemical functional group, applying a potential to said electrode sufficient to generate reagents, removing the protected group, coupling a reagent to the deprotected group to form a monomer (col. 1, lines 47-54).

Claim 6 is rejected because SOUTHERN discloses protected monomers or preformed molecules having protected chemical functional groups at non-bonding sites in col. 5, lines 10-20.

Claims 7 and 8 are rejected because SOUTHERN further discloses amino acid as the monomer and nucleic acid as the performed molecule in col.4, line 26.

Claim 9 is rejected because the reference discloses the use of linker molecules or monomers in col. 6, line 21.

Claim 11 is rejected because SOUTHERN further teaches that the molecule is directly attached to the surface of said substrate, via a linker molecule or attached to a layer of material overlaying said substrate in col. 6, lines 20-26.

Claim 12 is rejected because SOUTHERN teaches the protection of the chemical functional groups with an acid or base labile protecting group at col. 7, lines 1-5 and 25-28 and in claim 4 of the reference.

Claims 13 and 14 are rejected as SOUTHERN teaches the use of an array of electrodes in col. 7, line 3 and said array comprising at least 100 electrodes at col. 7, line 61.

Claim 15 is rejected as the combinatorial synthesis method of SOUTHERN discloses sequentially deprotecting other protected chemical functional group of the monomer or pre-formed molecule and bonding another monomer or pre-formed molecule to the deprotected monomer in col. 7, lines 5-22 and in claim 6, steps c,d of the reference.

Claim Rejections - 35 USC § 103

3. Claims 1-9 and 11-51 are rejected under 35 U.S.C. 103(a) as being unpatentable over HELLER et al. US 5,929,208 in view of SOUTHERN US 5,667,667.

HELLER et al. teach an electrophoretic synthesis of polymers wherein the method comprises providing a plurality of reaction locations on a porous substrate, each reaction location being individually electronically addressable and proximate to at least one molecule bearing at least one protected chemical functional group, applying a potential to said electrode sufficient to generate reagents, removing the protected group, coupling a reagent to the deprotected group to form a monomer (col. 39, lines 35-48; col. 40, lines 1-35).

The difference between the HELLER method and that of Applicant's is that HELLER employs an electrophoretic technique while Applicant teaches an electrochemical method of combinatorial synthesis.

The deficiency in HELLER is disclosed by the secondary reference to SOUTHERN who teaches a method for electrochemical placement of a material at a specific location on a substrate array which comprises the steps of providing a substrate having at its surface at least one electrode that is proximate to at least one molecule bearing at least one protected chemical functional group (col. 10, lines 52-57); applying a potential to said electrode sufficient to generate electrochemical reagents capable of deprotecting at least one of the protected chemical functional groups of said molecule (col. 10, lines 59-61; col. 6, lines 47-49) producing a chemical reaction thereby and

bonding the deprotected chemical functional group with a monomer or a pre-formed molecule (col. 10, lies 62-64).

HELLER and SOUTHERN in combination teach all of the limitations of Applicant's independent claims 1 and 47.

It would have been obvious to one of skill in the art at the time the invention was made to have modified the HELLER method by employing an electrochemical technique instead of an electrophoretic combinatorial synthesis as taught by SOUTHERN because SOUTHERN has shown that the use of an electrochemical technique would have provided the necessary stringency control allowing for self-addressable areas of specific and non-specific binding interactions, further providing more control of the synthesis by protective and deprotective techniques adaptable to the electrochemical process which prevents the occurrence of cross-talk associated with spatial distribution of electric fields characteristic of electrophoretic processes - therefore improving the end quality of the polymer thus formed.

Independent claims 16 and 41 are also rejected as HELLER teaches a repeating of steps of biasing and charging active sites of the substrate array so as to synthesize a set of oligomers (col. 40, lines 2-6, 25-32). The secondary reference to SOUTHERN also teaches repeating of the steps of applying voltage and depositing/bonding protected monomers so as to synthesize a set of oligomers at col. 10, lines 65-67.

Claims 45 and 46 are rejected as SOUTHERN further discloses the use of a gettering structure in the form of a ring shaped counter electrode at col. 11, lines 7-9.

It would have been obvious to one of skill in the art at the time of the invention to have modified HELLER with the electrochemical synthesis and use of a gettering structure taught by SOUTHERN in HELLER because SOUTHERN has shown that the use of the gettering structures / electrodes at sufficient low voltage would have controlled side reactions during synthesis, thus minimizing formation of bubbles to provide more stability in the reaction rate and electrolytic environment.

HELLER et al. teach all of the specific limitations of the dependent claims and can be combined with SOUTHERN as each are from the same technology area of combinatorial synthesis.

Claims 2, 18, 43 and 48 are rejected because HELLER et al. disclosed the placing of a buffer solution in contact with the electrode at the surface of the substrate to prevent electrochemically generated reagents from leaving the locality of the electrode (col. 22, lines 25-37).

Claims 3, 19 and 49 are rejected because Heller et al. disclose the use of a phosphate buffer at col. 22, line 41 of the reference.

Claims 4, 20 and 50 are rejected as the primary reference to HELLER discloses that the buffering solution is present in a concentration of at least 0.01 mM at col. 22, line 40.

Claims 5, 21 and 51 are also rejected as the primary prior art discloses that the buffering solution is present in a concentration range of 0.1 to 100 mM at col. 22, line 40.

Claim 6 is rejected as Heller discloses protected monomers or preformed molecules having protected chemical functional groups at non-bonding sites in col. 15, lines 48-58.

Claims 7 and 22 are rejected because the primary reference to HELLER further discloses amino acid as the monomer in col.21, line 30. (also see col. 6, lines 24-41)

Claims 8, 37 and 44 are rejected as Heller et al. employ pre-formed molecules selected from the group consisting of proteins, nucleic acids, polysaccharides and porphyrins (col.17, lines. 1-7). (also see col. 6, lines 24-41)

Claims 9 and 23 are rejected because the reference discloses the use of linker molecules or monomers in col. 21, lines 10-16.

Claims 11 and 24 are rejected as the molecule of Heller et al. is directly attached to the surface of said substrate, via a linker molecule or attached to a layer of material overlaying said substrate in col. 14, lines 56-67.

Claims 12 and 27 are rejected because Heller et al. teach the protection of the chemical functional groups with an acid or base labile protecting group at col. 20, lines 25-35.

Claims 13, 14, 29-31 and 40 are rejected as Heller et al. teach the use of an array of electrodes in col. 4, lines 44-54

Claim 15 is rejected as the combinatorial synthesis method of Heller et al. discloses sequentially deprotecting other protected chemical functional group of the monomer or pre-formed molecule and bonding another monomer or pre-formed molecule to the deprotected monomer in col. 15, lines 48-58.

Claims 17, 42 and 47 are rejected as the primary reference teaches selective deprotection by the application of potential to one or more electrodes sufficient to generate electrochemical reagents a the selected electrodes in col. 15, lines 48-58.

Claim 25 is rejected as HELLER et al. teach the use of glass as overlaying layers in col. 10, lines 5-8, 47-52; col. 17, lines 6-10.

Claim 26 is rejected as HELLER et al. teach the method wherein the linker molecule comprises a group cleavable by an electrochemically generated reagent, which cleavable group enables removal from said substrate of one or more bonded molecules (col. 39, lines 21-25).

Claim 28 is rejected as the substrate used in the prior art may be a semiconductor, plastic, glass or ceramic substrate in col. 10 lines 5-8.

Claim 32 is rejected as the microcapillary electrode tubes of Heller et al. have diameters in the range of 1-100μ (col. 22, lines 28-30).

Claim 33 is rejected as Heller et al. teach the use of platinum electrodes (col. 14, lines 34-36).

With regard to claim 34, although neither of the references provide for a preloading of the electrode with hydrogen, it is the Examiner's position that this appears to be a matter of designer choice of embodiment as HELLER teaches an exposure of the electrode to oxide and hydroxyl groups in aqueous solution in Example 5 and does not appear to significantly alter the overall method of the prior art, absent evidence to the contrary. However, should claim 1 be found allowable, the instant rejected claim dependent thereupon, albeit designer choice of embodiment, would be allowable.

Claim 35 is rejected as Southern teaches capping the molecule with acetic anhydride col. 6, lines 35-36. It would have been obvious to a person of skill to have used the capping monomers of SOUTHERN in HELLER as SOUTHERN teaches that the capping would have achieved the desired results of controlling the electrochemical reaction.

Claims 36 and 38 are rejected as the Heller et al. method teaches additional bonding steps wherein pre-formed molecules are bonded to deprotected chemical functional groups, said pre-formed molecule bearing at least one protected chemical functional group in claims 6 and 8 of the reference.

Claim 39 is rejected as the electrode pads of Heller et al. are packaged with a switch box for selective activation (col. 25, lines 1-3).

Response to Amendment

4. The 102(e) Rejection of the Claims 1-34, 36-44 and 47-51 over HELLER et al. US 5,929,508 has been **withdrawn** for the reasons below and a new grounds for rejection has been made.

5. The 103(a) Rejection of claim 35 over HELLER et al. and SOUTHERN has been **maintained** as indicated above.

6. The 103(a) Rejection of claims 45 and 46 over HELLER et al. in further view of SAVERY US 4,280, 885 has been **withdrawn** for the reasons below and a new grounds of rejection has been made.

7. The objection to claim 10 has been **withdrawn** in view of Applicant's cancellation thereof.

8. The double patenting rejection of claims 1-51 over claims 1-49 of Applicant's co-pending applications serial no. 09/003075 now US Patent 6,093,302 and 09/394138 pending, has been **maintained.** Applicants' indication of their willingness to submit a Terminal Disclaimer upon the indication of Allowable Subject matter has been made of record.

Response to Arguments

9. Applicant's arguments with respect to claims 1-51 have been considered but are moot in view of the new ground(s) of rejection.

It is noted, however, that the Examiner particularly agrees with the significant differences between the electrophoretic synthesis of the HELLER et al. method (US 5,929,208) and the electrochemical synthesis of instant invention as pointed out by Applicants:

- The HELLER method uses electric fields to transport charged reagents to reaction sites while Applicant uses electrochemically generated reagents:
- HELLER uses electric fields to transport charged moieties, while Applicant uses selectively charged electrodes in an array for charging ions for transport to certain sites, employing the use of charged or uncharged reagents and reagent precursors.

As the HELLER process is an electrophoretic process, the limitations thereof include the inability to use protecting groups to protect the reactive functional groups at the microlocations since there is no mechanism for removing the protective groups resulting in various binding entities or reactants migrating throughout the solution. This migration coupled with the spatial distribution of the electric fields inherent to electrophoresis compromises the integrity of the electrophoretically synthesized polymer. Applicant's invention offers an improvement over the prior art technique as it allows for more control of the synthesis by protective and deprotective techniques compatible with the electrochemical process which prevents the occurrence of cross-talk associated with spatial distribution of electric fields characteristic of electrophoresis, therefore improving the end quality of the polymer thus formed.

Applicant may urge that HELLER's use of buffering agents and the specific polymers and deblocking agents employed in the electrophoretic process does not read over Applicant's use of same in an electrochemical process. In response, the fact that applicant has recognized another advantage which would flow naturally from following the suggestion of the prior art combination teachings of SOUTHERN and HELLER

cannot be the basis for patentability when the differences would otherwise be obvious. See *Ex parte Obiaya*, 227 USPQ 58, 60 (Bd. Pat. App. & Inter. 1985).

While Applicant's arguments were persuasive in overcoming the rejection of the claims over HELLER et al. alone, the arguments were not persuasive to overcome the new rejection of HELLER in view of SOUTHERN as SOUTHERN expressly teaches a method for electrochemical combinatorial synthesis of an array of separately formed polymers wherein an electric potential is applied to an array of electrodes proximate to one or more protected, chemical-functional-group bearing molecules to generate electrochemical reagents at selected electrodes of the array for deprotecting the functional groups and subsequently bonding of additional monomers.

Accordingly, claims 1-51 fail to distinguish over the prior art.

Conclusion

10. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. DURST et al. US 6,086,748; KIRK et al. US 5,798,035 and TEOULE et al. US 5,837,859 who all teach electrochemical combinatorial polymer synthesis.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Erica Smith-Hicks whose telephone number is 703/ 305-7645. The examiner can normally be reached on Mon.-Thurs. 8:30 a.m.-6:00 p.m. and alternate Fridays from 8:30 a.m.-5:00 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Kathryn Gorgos can be reached on 703/ 308-3328. The fax phone numbers for the organization where this application or proceeding is assigned are 703/ 305-7719 for regular communications and 703/ 305-3599 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703/ 308-0661.

ESH
October 18, 2000

Kathryn Gorgos
Supervisory Patent Examiner
Technology Center 1700